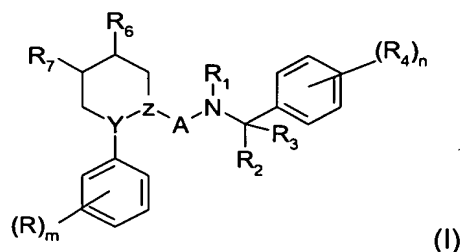


In the Claims:

Please amend claim 26 as follows. Please add new claims 67-77.

1. (Currently Amended) A compound of formula (I)



wherein

R is halogen or C_{1-4} alkyl;

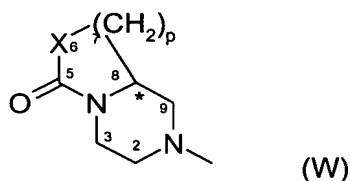
R_1 is C_{1-4} alkyl;

R_2 or R_3 independently are hydrogen or C_{1-4} alkyl;

R_4 is trifluoromethyl, C_{1-4} alkyl, C_{1-4} alkoxy, trifluoromethoxy or halogen;

R_5 represents hydrogen, C_{1-4} alkyl or C_{3-7} cycloalkyl;

R_6 is hydrogen and R_7 is a radical of formula (W):



or R_6 is a radical of formula (W) and R_7 is hydrogen;

X is CH_2 , NR_5 or O ;

Y is Nitrogen and Z is CH or Y is CH and Z is Nitrogen;

A is $C(O)$ or $S(O)_q$, provided that when Y is nitrogen and Z is CH , A is not $S(O)_q$;

m is zero or an integer from 1 to 3;

n is an integer from 1 to 3;

p and q are independently an integer from 1 to 2;

or a pharmaceutically acceptable salt or solvate thereof.

2. (Previously Presented) A compound as claimed in claim 1 R_6 is hydrogen, R_7 is a radical of formula (W) and Y is CH and Z is nitrogen.

3. (Previously Presented) A compound as claimed in claim 1 wherein A is $C(O)$.

4. (Previously Presented) A compound as claimed in claim 1 wherein X is CH₂.
5. (Previously Presented) A compound as claimed in claim 1 wherein p is 1.
6. (Previously Presented) A compound as claimed in claim 1 wherein each R₄ is independently trifluoromethyl group or halogen and n is 2.
7. (Previously Presented) A compound as claimed in claim 1 wherein each R is independently a halogen or a C₁₋₄ alkyl group, wherein m is 0, 1 or 2.
8. (Previously Presented) A compound as claimed in claim 1 wherein R₆ is hydrogen, R₇ is a radical of formula (W) and Y is CH and Z is nitrogen.
9. (Previously Presented) A compound as claimed in claim 1 wherein R₆ is hydrogen, R₇ is a radical of formula (W) and Y is CH and Z is nitrogen.
10. (Previously Presented) A compound selected from :
2-(R)-(4-Fluoro-2-methyl-phenyl)-4-(S)-(6-oxo-hexahydro-pyrrolo[1,2-*a*]-pyrazin-2-yl)-piperidine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methylamide;
2-(R)-(4-Fluoro-2-methyl-phenyl)-4-(S)-(6-oxo-hexahydro-pyrrolo[1,2-*a*]-pyrazin-2-yl)-piperidine-1-carboxylic acid[1-(R)-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-methylamide;
1-(4-Fluoro-2-methyl-phenyl)-4-(6-oxo-hexahydro-pyrrolo[1,2-*a*]pyrazin-2-yl)-piperidine-2-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
and enantiomers, diastereoisomers, and pharmaceutically acceptable salts or solvates thereof.
11. (Previously Presented) A compound selected from :
2-(R)-(4-Fluoro-2-methyl-phenyl)-4-(S)-((8aS)-6-oxo-hexahydro-pyrrolo[1,2-*a*]-pyrazin-2-yl)-piperidine-1-carboxylic acid [1-(R)-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-methylamide;
2-(R)-(4-Fluoro-2-methyl-phenyl)-4-(S)-((8aR)-6-oxo-hexahydro-pyrrolo[1,2-*a*]-pyrazin-2-yl)-piperidine-1-carboxylic acid [1-(R)-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-methylamide;

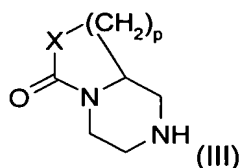
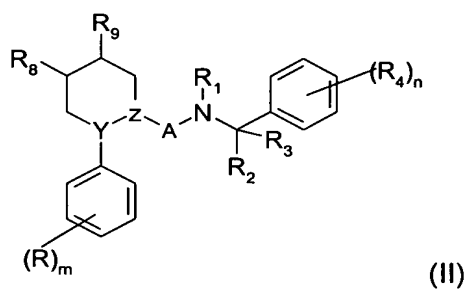
and amorphous and crystalline forms thereof and pharmaceutically acceptable salts or solvates thereof.

12-14. (Cancelled)

15. (Previously Presented) A pharmaceutical composition comprising a compound as claimed in claim 1 in admixture with one or more pharmaceutically acceptable carriers or excipients.

16. (Canceled)

17. (Previously Presented) A process for the preparation of a compound as claimed in claim 1 comprising reacting a compound of formula (II) wherein R_8 is =O and R_9 is hydrogen or R_8 is hydrogen and R_9 is =O



with compound of formula (III) or a salt thereof in the presence of a suitable metal reducing agent, followed where necessary or desired by one or more of the following steps:

- i) removal of any protecting group;
- ii) isolation of the compound as a salt or a solvate thereof;
- iii) separation of a compound of formula (I) or derivative thereof into the enantiomers thereof.

18. (Previously Presented) A compound as claimed in claim 1 wherein R_6 is a radical of formula (W), R_7 is a hydrogen and Y is nitrogen and Z is CH.

19. (Previously Presented) A compound as claimed in claim 1 wherein R₆ is a radical of formula (W), R₇ is a hydrogen and Y is nitrogen and Z is CH; A is C(O) and X is CH₂.

20. (Previously Presented) A compound as claimed in claim 1 wherein R₆ is a radical of formula (W), R₇ is a hydrogen, Y is nitrogen, Z is CH, A is C(O), X is CH₂, R is independently a halogen or a C₁₋₄ alkyl group, R₄ is a trifluoromethyl group, m is 1 or 2, n is 2 and p is 1.

21. (Previously Presented) 2-(R)-(4-Fluoro-2-methyl-phenyl)-4-(S)-(6-oxo-hexahydro-pyrrolo[1,2-*a*]-pyrazin-2-yl)-piperidine-1-carboxylic acid[1-(R)-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-methanamide and enantiomers, diastereoisomers, and pharmaceutically acceptable salts or solvates thereof.

22. (Previously Presented) A method for the treatment of a condition mediated by a tachykinin in a mammal comprising administering an effective amount of a compound as claimed in claim 1.

23. (Previously Presented) The method as claimed in claim 21, wherein said tachykinin is substance P.

24. (Previously Presented) The method as claimed in claim 21, wherein said mammal is man.

25. (Previously Presented) The method as claimed in claim 21, wherein said compound is selected from

2-(R)-(4-Fluoro-2-methyl-phenyl)-4-(S)-(6-oxo-hexahydro-pyrrolo[1,2-*a*]-pyrazin-2-yl)-piperidine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methanamide;

2-(R)-(4-Fluoro-2-methyl-phenyl)-4-(S)-(6-oxo-hexahydro-pyrrolo[1,2-*a*]-pyrazin-2-yl)-piperidine-1-carboxylic acid[1-(R)-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-methanamide;

1-(4-Fluoro-2-methyl-phenyl)-4-(6-oxo-hexahydro-pyrrolo[1,2-*a*]pyrazin-2-yl)-piperidine-2-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methanamide;

and enantiomers, diastereoisomers, and pharmaceutically acceptable salts or solvates thereof.

26. (Currently Amended) A method for the treatment of a CNS disorder mediated by substance P in a man comprising administering an effective amount of a compound as claimed in claim 1.

27. (Previously Presented) The method according to claim 26, wherein said CNS disorder is selected from depressive states and anxiety.

28. (Previously Presented) The method according to claim 27, wherein said depressive state is selected from
bipolar depression,
unipolar depression,
single or recurrent major depressive episodes,
recurrent brief depression with or without psychotic features, catatonic features,
melancholic features, weight loss, atypical features,
anxious depression,
cyclothymic or postpartum onset,
dysthymic disorder with early or late onset and with or without atypical features;
neurotic depression;
post traumatic stress disorders;
social phobia;
dementia of the Alzheimer's type, with early or late onset, with depressed mood;
vascular dementia with depressed mood;
mood disorders induced by alcohol, amphetamines, cocaine, hallucinogens,
inhalants, opioids, phencyclidine, sedatives, hypnotics, anxiolytics and other
substances;
schizoaffective disorder of the depressed type;
adjustment disorder with depressed mood; and
major depressive disorders resulting from a general medical condition.

29. (Previously Presented) The method as claimed in claim 26, wherein said CNS disorder is selected from
panic disorders with or without agoraphobia,

agoraphobia,
phobias,
obsessive-compulsive disorder,
post-traumatic stress disorders,
generalized anxiety disorders,
acute stress disorders, and
mixed anxiety-depression disorders.

30. (Previously Presented) The method as claimed in claim 26, wherein said compound is

2-(R)-(4-Fluoro-2-methyl-phenyl)-4-(S)-(6-oxo-hexahydro-pyrrolo[1,2-*a*]-pyrazin-2-yl)-piperidine-1-carboxylic acid[1-(R)-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-methanamide;
and enantiomers, diastereoisomers, and pharmaceutically acceptable salts or solvates thereof.

31. (Previously Presented) The method as claimed in claim 26, further comprising administering an effective amount of a serotonin reuptake inhibitor.

32. (Previously Presented) The method as claimed in claim 31, wherein said serotonin reuptake inhibitor is selected from fluoxetine, citalopram, femoxetine, fluvoxamine, paroxetine, indalpine, sertraline and zimeldine.

33. (Previously Presented) The method as claimed in claim 26, further comprising administering an effective amount of a dopaminergic antidepressant.

34. (Previously Presented) The method as claimed in claim 33, wherein said dopaminergic antidepressant is selected from bupropion and amineptine.

35. (Previously Presented) A method for the treatment of a major depressive disorder in man comprising administering an effective amount of 2-(R)-(4-Fluoro-2-methyl-phenyl)-4-(S)-(6-oxo-hexahydro-pyrrolo[1,2-*a*]-pyrazin-2-yl)-piperidine-1-carboxylic acid[1-(R)-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-methanamide, or an enantiomer, diastereoisomer, or pharmaceutically acceptable salt or solvate thereof.

36. (Previously Presented) The method as claimed in claim 35, wherein said major depressive disorder is selected from bipolar depression and unipolar depression.
37. (Previously Presented) The method as claimed in claim 35, further comprising administering an effective amount of a serotonin reuptake inhibitor selected from fluoxetine, citalopram, femoxetine, fluvoxamine, paroxetine, indalpine, sertraline and zimeldine.
38. (Previously Presented) The method as claimed in claim 35, further comprising administering an effective amount of a dopaminergic antidepressant selected from bupropion and amineptine.
39. (Previously Presented) A method for the treatment of anxiety in man comprising administering an effective amount of 2-(R)-(4-Fluoro-2-methyl-phenyl)-4-(S)-(6-oxo-hexahydro-pyrrolo[1,2-*a*]-pyrazin-2-yl)-piperidine-1-carboxylic acid[1-(R)-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-methanamide, or an enantiomer, diastereoisomer, or pharmaceutically acceptable salt or solvate thereof.
40. (Previously Presented) The method as claimed in claim 39, further comprising administering an effective amount of a serotonin reuptake inhibitor selected from fluoxetine, citalopram, femoxetine, fluvoxamine, paroxetine, indalpine, sertraline and zimeldine.
41. (Previously Presented) The method as claimed in claim 39, further comprising administering an effective amount of a dopaminergic antidepressant selected from bupropion and amineptine.
42. (Previously Presented) A method for the treatment of panic disorder in man comprising administering an effective amount of 2-(R)-(4-Fluoro-2-methyl-phenyl)-4-(S)-(6-oxo-hexahydro-pyrrolo[1,2-*a*]-pyrazin-2-yl)-piperidine-1-carboxylic acid[1-(R)-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-methanamide, or an enantiomer, diastereoisomer, or pharmaceutically acceptable salt or solvate thereof.

43. (Previously Presented) A method for the treatment of emesis in a mammal comprising administering an effective amount of a compound as claimed in claim 1.
44. (Previously Presented) The method as claimed in claim 43, wherein said mammal is man.
45. (Previously Presented) The method as claimed in claim 43, wherein said emesis is delayed emesis.
46. (Previously Presented) The method as claimed in claim 43, wherein said emesis is anticipatory emesis.
47. (Previously Presented) The method as claimed in claim 43, wherein said emesis is induced by cancer chemotherapeutic agents.
48. (Previously Presented) The method as claimed in claim 43, wherein said cancer chemotherapeutic agent is selected from cyclophosphamide, carmustine, lomustine, chlorambucil, dactinomycin, doxorubicin, mitomycin-C, bleomycin, cytarabine, methotrexate, 5-fluorouracil, etoposide, vinblastine, vincristine, cisplatin, dacarbazine, procarbazine, hydroxyurea and combinations thereof.
49. (Previously Presented) The method as claimed in claim 43, wherein said emesis is induced by radiation sickness or radiation therapy.
50. (Previously Presented) The method as claimed in claim 43, wherein said emesis is induced by pregnancy.
51. (Previously Presented) The method as claimed in claim 43, wherein said emesis is induced by post-operative sickness.
52. (Previously Presented) The method as claimed in claim 43, wherein said emesis is induced by migraine.

53. (Previously Presented) The method as claimed in claim 43, wherein said emesis is induced by opioid analgesics.
54. (Previously Presented) The method as claimed in claim 43, further comprising administering an effective amount of a 5HT3 antagonist.
55. (Previously Presented) The method as claimed in claim 54, wherein said 5HT3 antagonist is selected from ondansetron, granisetron and metoclopramide.
56. (Previously Presented) The method as claimed in claim 43, wherein said compound is
2-(R)-(4-Fluoro-2-methyl-phenyl)-4-(S)-(6-oxo-hexahydro-pyrrolo[1,2-*a*]-pyrazin-2-yl)-piperidine-1-carboxylic acid[1-(R)-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-methanamide;
and enantiomers, diastereoisomers, and pharmaceutically acceptable salts or solvates thereof.
57. (Previously Presented) The method as claimed in claim 56, further comprising administering an effective amount of a 5HT3 antagonist selected from ondansetron, granisetron and metoclopramide.
58. (Previously Presented) A method for the treatment of emesis in man comprising administering an effective amount of 2-(R)-(4-Fluoro-2-methyl-phenyl)-4-(S)-(6-oxo-hexahydro-pyrrolo[1,2-*a*]-pyrazin-2-yl)-piperidine-1-carboxylic acid[1-(R)-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-methanamide, or an enantiomer, diastereoisomer, or pharmaceutically acceptable salt or solvate thereof.
59. (Previously Presented) A method for the treatment of sleep disorders in man comprising administering an effective amount of a compound as claimed in claim 1.
60. (Previously Presented) A method for the treatment of dependence on a substance selected from nicotine, alcohol, caffeine, phencyclidine phencyclidine-like compounds, opiates, benzodiazepines, cocaine, sedative drugs, hypnotic drugs,

amphetamines, amphetamine-related drugs, and combinations thereof; in man, comprising administering an effective amount of a compound as claimed in claim 1.

61. (Previously Presented) The pharmaceutical composition as claimed in claim 15, further comprising a serotonin reuptake inhibitor.

62. (Previously Presented) The pharmaceutical composition as claimed in claim 15, wherein said serotonin reuptake inhibitor is selected from fluoxetine, citalopram, femoxetine, fluvoxamine, paroxetine, indalpine, sertraline and zimeldine.

63. (Previously Presented) The pharmaceutical composition as claimed in claim 15, further comprising a dopaminergic antidepressant.

64. (Previously Presented) The pharmaceutical composition as claimed in claim 63, wherein said dopaminergic antidepressant is selected from bupropion and amineptine.

65. (Previously Presented) The pharmaceutical composition as claimed in claim 15, further comprising a 5HT3 antagonist.

66. (Previously Presented) The pharmaceutical composition as claimed in claim 65, wherein said 5HT3 antagonist is selected from ondansetron, granisetron and metoclopramide.

67. (New) 2-(R)-(4-Fluoro-2-methyl-phenyl)-4-(S)-((8aS-6-oxo-hexahydro-pyrrolo[1,2-*a*]-pyrazin-2-yl)-piperidine-1-carboxylic acid[1-(R)-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-methylamide hydrochloride.

68. (New) 2-(R)-(4-Fluoro-2-methyl-phenyl)-4-(S)-((8aS-6-oxo-hexahydro-pyrrolo[1,2-*a*]-pyrazin-2-yl)-piperidine-1-carboxylic acid[1-(R)-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-methylamide hydrochloride as anhydrous crystalline form.

69. (New) The method as claimed in claim 26, wherein said compound is

2-(R)-(4-Fluoro-2-methyl-phenyl)-4-(S)-((8aS-6-oxo-hexahydro-pyrrolo[1,2-*a*]-pyrazin-2-yl)-piperidine-1-carboxylic acid[1-(R)-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-methylamide hydrochloride.

70. (New) A method for the treatment of a major depressive disorder in man comprising administering an effective amount of 2-(R)-(4-Fluoro-2-methyl-phenyl)-4-(S)-((8aS-6-oxo-hexahydro-pyrrolo[1,2-*a*]-pyrazin-2-yl)-piperidine-1-carboxylic acid[1-(R)-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-methylamide hydrochloride.

71. (New) A method for the treatment of anxiety in man comprising administering an effective amount of 2-(R)-(4-Fluoro-2-methyl-phenyl)-4-(S)-((8aS-6-oxo-hexahydro-pyrrolo[1,2-*a*]-pyrazin-2-yl)-piperidine-1-carboxylic acid[1-(R)-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-methylamide hydrochloride.

72. (New) A method for the treatment of panic disorder in man comprising administering an effective amount of 2-(R)-(4-Fluoro-2-methyl-phenyl)-4-(S)-((8aS-6-oxo-hexahydro-pyrrolo[1,2-*a*]-pyrazin-2-yl)-piperidine-1-carboxylic acid[1-(R)-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-methylamide hydrochloride.

73. (New) 2-(R)-(4-Fluoro-2-methyl-phenyl)-4-(S)-((8aR)-6-oxo-hexahydro-pyrrolo[1,2-*a*]-pyrazin-2-yl)-piperidine-1-carboxylic acid[1-(R)-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-methylamide hydrochloride.

74. (New) The method as claimed in claim 26, wherein said compound is 2-(R)-(4-Fluoro-2-methyl-phenyl)-4-(S)-((8aR)-6-oxo-hexahydro-pyrrolo[1,2-*a*]-pyrazin-2-yl)-piperidine-1-carboxylic acid[1-(R)-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-methylamide hydrochloride.

75. (New) A method for the treatment of a major depressive disorder in man comprising administering an effective amount of 2-(R)-(4-Fluoro-2-methyl-phenyl)-4-(S)-((8aR)-6-oxo-hexahydro-pyrrolo[1,2-*a*]-pyrazin-2-yl)-piperidine-1-carboxylic acid[1-(R)-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-methylamide hydrochloride.

76. (New) A method for the treatment of anxiety in man comprising administering an effective amount of 2-(R)-(4-Fluoro-2-methyl-phenyl)-4-(S)-((8aR)-6-oxo-

hexahydro-pyrrolo[1,2-*a*]-pyrazin-2-yl)-piperidine-1-carboxylic acid[1-(R)-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-methanamide hydrochloride.

77. (New) A method for the treatment of panic disorder in man comprising administering an effective amount of 2-(R)-(4-Fluoro-2-methyl-phenyl)-4-(S)-((8aR)-6-oxo-hexahydro-pyrrolo[1,2-*a*]-pyrazin-2-yl)-piperidine-1-carboxylic acid[1-(R)-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-methanamide hydrochloride.